

REMARKS

Claims 13, 24, and 29-71 were pending in the present application. Claims 31, 34, 35, and 70 have been have been amended. Accordingly, after the amendments presented herein have been entered, claims 13, 24 and 29-71 will remain pending.

Support for the new claims and the claim amendments presented herein can be found throughout the specification, including the originally filed claims.

No new matter has been added. Any amendments to and/or cancellation of the claims should in no way be construed as an acquiescence to any of the Examiner's rejections and was done solely to expedite the prosecution of the application. Applicants reserve the right to pursue the claims as originally filed in this or a separate application(s).

Rejection of Claims 34-37 and 44-67 Under 35 U.S.C. §112, Second Paragraph

The Examiner has rejected claims 34-37 and 44-67 under 35 U.S.C. §112, second paragraph, "as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention." In particular, the Examiner is of the opinion that

[c]laims 34, 35 and their dependents are drawn to a method of identifying compounds, however are rendered vague and indefinite for reciting "capable of" because it is unclear if the compounds must prevent fertilization or merely may potentially prevent fertilization. Moreover, it is unclear how one would identify a compound that might have a desired activity.

Applicants respectfully traverse the foregoing rejection. However, in an effort to expedite prosecution and in no way acquiescing to the Examiner's rejection, Applicants have amended claims 34 and 35 so that they are directed to methods for identifying a candidate compound which prevents fertilization in a subject. Applicants respectfully submit that the claimed methods still identify the same compounds as the claims prior to amendment, and therefore the claim amendments are non-limiting. Accordingly, Applicants respectfully request reconsideration and withdrawal of the foregoing rejection.

The Examiner is also of the opinion that “claims 34-37 and their dependents are drawn to methods for identifying compounds, however are rendered vague and indefinite.”

Applicants respectfully traverse the foregoing rejection. Applicants respectfully submit that claims 34-37 are directed to methods for identifying a candidate compound which prevents fertilization or may be used as a contraceptive in a subject comprising *contacting MSH5 with a test compound*; and assaying for modulation of the *expression or activity of MSH5* in the presence of said test compound, wherein inhibition of the expression or activity of MSH5 by the test compound identifies the test compound as a candidate compound which prevents fertilization or may be used as a contraceptive in a subject.

The Examiner is of the opinion that the claims are vague and indefinite based on the phrase “assaying for modulation,” and that it is “unclear if candidate compounds that inhibit or stimulate expression of MSH5 are being assayed, or if the expression of MSH2 (*sic*) is being assayed.” The claims require contacting MSH5 with a test compound and determining a change in the *expression or activity of MSH5 in the presence of the test compound*, and then identifying a test compound as a candidate compound if the compound inhibits expression of activity of MSH5. Applicants respectfully submit that the claims clearly require that the expression or activity of *MSH5* is assayed. Therefore, Applicants respectfully submit that the phrase “assaying for modulation” does not render the claims indefinite.

Accordingly, the pending claims comply with 35 U.S.C. §112, second paragraph. Based on the foregoing, Applicants’ respectfully request reconsideration and withdrawal of the foregoing rejection.

Rejection of Claims 13, 24, and 29-71 Under 35 U.S.C. §103(a)

The Examiner has rejected claims 13, 24, and 29-71 under 35 U.S.C. §103(a) as being unpatentable over Fishel *et al.* (U.S. Patent No. 6,333,153) in view of Hollingsworth (Genes & Development, 1995). In particular, the Examiner is of the opinion that

Hollingsworth teaches that MSH5 is a meiosis specific gene, active to facilitate meiosis and meiotic chromosome synapsis (abstract) in bacteria, yeast and humans (p. 1729). Hollingsworth additionally teaches that mutant MSH5 (or inhibited activity thereof) results in decreased spore (or gamete) viability (p. 1735, 1736). Moreover, Hollingsworth suggests that inhibited or reduced activity of MSH5 inhibits meiosis, chromosome synapsis and decreases fertility. At the time of the claimed invention, it would have been obvious to one of ordinary skill in the art to use inhibitors of MSH5 activity identified by the methods of Fishel, as inhibitors of meiosis, chromosome synapsis and fertility, since the gene was known to facilitate these activities. It would have been further obvious to one of ordinary skill in the art to identify the inhibitors useful for contraceptive agents, since it was well known in the art that meiosis, chromosome synapsis and fertility are required for conception. Moreover, at the time of the claimed invention, one of ordinary skill in the art would have been motivated by the teachings of Hollingsworth to use the identified compounds of Fishel, as inhibitors of meiosis, fertilization and chromosome synapsis, as well as contraceptive agents.

Applicants respectfully traverse the foregoing rejection for the following reasons.

To establish a *prima facie* case of obviousness, it is necessary for the Examiner to present evidence, preferably in the form of some teaching, suggestion, incentive or inference in the applied references, or in the form of generally available knowledge, that one having ordinary skill in the art would have been motivated to make the claimed invention and would have had a reasonable expectation of success in making the claimed invention. Under section 103, "[b]oth the suggestion and the expectation of success must be founded in the prior art, not in applicant's disclosure" (*Amgen, Inc. v. Chugai Pharmaceutical Co., Ltd.* 927 F.2d 1200, 1207, 18 USPQ2d 1016 (Fed. Cir. 1991), quoting *In re Dow Chemical Co.*, 837 F.2d 469, 473, 5 USPQ2d 1529, 1531 (Fed Cir. 1988)). Moreover, when a combination of references are used to establish a *prima facie* case of obviousness, the Examiner must present evidence that one having ordinary skill in the art would have been motivated to combine the teachings in the applied references in the proposed manner to arrive at the claimed invention. See, e.g., *Carella v. Starlight Archery*, 804 F.2d 135, 231 USPQ 644 (Fed. Cir. 1986); and *Ashland Oil, Inc. v. Delta Resins and Refractories, Inc.*, 776 F.2d 281, 227 USPQ 657 (Fed. Cir. 1985). ***Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations***

(M.P.E.P. 2143).

Applicants respectfully traverse the foregoing rejection. Specifically, Fishel *et al.* fail to teach or suggest **any** association between MSH5, and contraception, fertilization, or meiosis. Nor do Fishel *et al.* teach or suggest methods for identifying candidate compounds useful for inhibiting meiosis, compounds useful as contraceptives, or compounds which prevent fertilization. Thus, the primary reference of Fishel *et al.* relied upon by the Examiner fails to teach or suggest the claimed invention.

Furthermore, Applicants respectfully submit that the secondary reference of Hollingsworth *et al.* relied on by the Examiner fails to make up for the above stated deficiencies in the primary reference of Fishel *et al.*

The present invention is based upon the discovery that *Msh5*^{-/-} mice, *i.e.*, mice with a null mutation in *Msh5*, are viable, but are sterile and that MSH5 is required for chromosome pairing and/or synapsis (see Example 1). The instant specification further teaches methods for identifying compounds which inhibit meiosis, compounds useful as contraceptives, or compounds which prevent fertilization.

Hollingsworth *et al.* describe the identification of the MSH5 gene **in yeast**, and identify it as a MutS homolog. Hollingsworth *et al.* present data relating to the **yeast** protein and its effects on spore viability. Hollingsworth *et al.* state that the role of MSH5 is in facilitating cross-overs between homologs during meiosis based on data in yeast. In addition, Hollingsworth concludes that MSH5 is not involved in mismatch repair.

As is known in the art, homology between yeast and mammalian proteins alone is insufficient to determine the function of a molecule. In contrast to the instant application, Hollingsworth *et al.* **does not conclusively set forth any function of a mammalian MSH5 molecule**. In the instant Office Action, the Examiner has stated that “Hollingsworth teaches that MSH5 is a meiosis specific gene, active to facilitate meiosis and meiotic chromosome synapsis (abstract) in bacteria, yeast and humans (p. 1729).” However, Hollingsworth *et al.* do not teach or suggest that MSH5 is involved in meiosis in bacteria or humans. Hollingsworth state only

that “***MutS homologs*** function in mismatch repair in a variety of different organisms, including bacteria, yeast and humans” (p. 1729). Hollingsworth *et al.* do not conclusively teach or suggest that MSH5 functions in the same manner as other MutS homologs. Furthermore, Hollingsworth *et al.* fail to teach or suggest that a compound which inhibits MSH5 could be used to inhibit fertilization in a subject, *i.e.*, act as a contraceptive compound.

Furthermore, nowhere do Hollingsworth *et al.* teach or suggest methods for identifying candidate compounds useful for inhibiting meiosis, compounds useful as contraceptives, or compounds which prevent fertilization. Thus, Hollingsworth *et al.*, in combination with Fishel *et al.* fail to teach or suggest Applicants’ invention.

Accordingly, Applicant respectfully request reconsideration and withdrawal of the rejection of claims 13, 24, and 29-71 under 35 U.S.C. §103(a).

Previous Rejection Under 35 U.S.C. §103(a)

In the Office Action dated December 31, 2002, the Examiner rejected claims 31 and 32 under 35 U.S.C. §103(a) as being unpatentable over Fishel *et al.* (U.S. Patent No. 6,333,153) in view of Winand *et al.* In the instant Office Action, the Examiner has stated that the arguments presented in Applicants’ Amendment and Response dated January 27, 2004 “fail to persuade” based on the present rejection of the claims based on Hollingsworth *et al.* and that “the affidavits filed on January 27, 2004 under 37 C.F.R. 1.131 are not signed, and are therefore defective.”

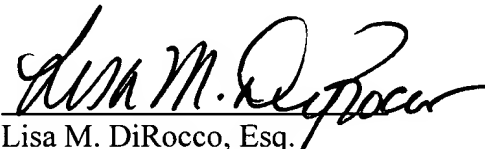
Applicants respectfully submit that executed Declarations Under 37 C.F.R. §1.131 will be submitted as soon as possible in order to obviate the previous rejection of claims 31 and 32 under 35 U.S.C. §103(a) as being unpatentable over Fishel *et al.* (U.S. Patent No. 6,333,153) in view of Winand *et al.*

CONCLUSION

In view of the amendments set forth above, it is respectfully submitted that this application is in condition for allowance. If there are any remaining issues or the Examiner believes that a telephone conversation with Applicants' Attorney would be helpful in expediting prosecution of this application, the Examiner is invited to call the undersigned at (617) 227-7400.

Respectfully submitted,

LAHIVE & COCKFIELD, LLP

A handwritten signature in black ink, appearing to read "Lisa M. DiRocco", is written over a horizontal line.

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